UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,486	11/29/2000	Takehiro Yatomi	1110-0280P	1332

2292 7590 05/08/2002

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	8

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/701,486	Applicant(s) YATOMI, TAKEHIRO	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, and 5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Claim 4 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7B, filed March 5, 2002.

Specification

1. The abstract of the disclosure is objected to because it does not reflect that the invention is focusing on a method of using the preventatives or remedies, rather than the substances themselves. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim1-3 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being potentially enabling for prevention of some autoimmune demyelinating diseases using some substances, does not reasonably enable the prevention of all such diseases with any apoptosis-suppressing substances. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

While the art does recognize that multiple sclerosis (or its experimental model EAE) may be prevented (see. e.g. Elliot et al., J. Clin. Invest. Vol. 28, 1602- stating that work in the relevant field had shown that it was possible to prevent EAE in mice), especially insofar as prevention means to prevent relapse of the disease. See e.g., Elliot, p. 1602; Kennedy et al., J. Immun., vol.144, pp. 909-15, 909-10 (1990). However, in each of these references, the immunogen was a non-antibody protein. Antibodies have not been shown, and are therefore not known in the art, to be effective in preventing autoimmune diseases.

While treatment of an autoimmune demyelinating disease is enabled, the application has not shown that *any* substance that suppresses apoptosis could prevent these diseases. The applicant has defined prevention of a disease as to prevent the disease (i.e. to keep it from taking hold of a subject) or to prevent relapse in a treated subject. While the applicant has shown that the antibody used in the examples has some therapeutic value in the treatment of an autoimmune demyelinating disease, he has not shown that it could prevent the disease. The applicant has given examples of the use of an antibody in the treatment of rats. The examples show that administration of the antibody does have the effect of reducing the effect of the disease when used as an immunogen or a post-infection treatment. However, the immunized rats in the experiment did get the disease. Because the rats got the disease, the applicant has not shown that the claimed method is effective, at least as to embodiments where antibodies are the apoptosis-suppressing substance, as a preventative.

Further, while the art has developed experimental immunogens to the autoimmune diseases in mice, and has been successful in preventing relapse, the methods of these treatments did not involve antibodies to the apoptosis ligand, the molecule shown in the applicant's

examples, or even work administering apoptosis blocking agents. See, e.g., Kennedy et al., J. Imm. vol. 144, abstract (describing the immunogen used) and p. 911 (showing success in preventing relapse); and Nicholson et al., Immunity, vol. 3, abstract (describing the compound used), and p. 402 (stating the treatment works by stimulating the immune system). Rather, the art teaches that if prevention is to be achieved, it is done by preventing the immune system from becoming autoreactive, not by the administration of apoptosis blocking substances.

Therefore, while the applicant's claims may be enabled for methods of treatment, and in methods of helping to prevent relapse by administration to subjects wherein remission and relapse are repeated, he has not enabled one skilled in the art to perform a method wherein the diseases are prevented in the subject.

3. Claims 1, 6, and 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The application has described a method of treating an autoimmune demyelinating disease comprising use an antibody to the Fas ligand or an antagonist to Fas. However, claims 1, 6, and 7 encompass embodiments where the target of the apoptosis suppressing substance is not either Fas, or the Fas ligand. In the art, it is known that other cellular molecules are involved in the Fas apoptosis pathway. See generally, Holoshitz et al., U.S. Patent Number 6,098,631 (the '631 patent). The '631 patent discloses methods of treating autoimmune diseases, including multiple sclerosis, by inhibiting the Fas apoptosis pathway. See, '631, col. 1, lines 9-20, col. 5, lines 44-50, and col. 6, lines 57-62 (describing the Fas/sphingomyclin pathway and stating that the disclosed method of treatment may target any of

the members of the pathway). Because the applicant in this case has not described a method wherein any molecule other than Fas or Fas ligand is targeted, the applicant has not provided a written description for the claimed method insofar as it describes a method for treatment where the apoptosis suppressing substance is other than a Fas ligand antibody, or a Fas antagonist.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3 and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Keana et al., U.S. Patent Number 6,184,210. This patent discloses an apoptosis inhibitor useful in the treatment of multiple sclerosis. Col. 3, lines37-55. The reference also discloses the use of the substance as a preventative of Fas ligand induced apoptosis in mouse liver. Col. 23, lines 34-38. Thus, a person of ordinary skill in the art would have known to use the substance in the claimed method because of the effectiveness of the substance in preventing mouse liver cell lysis and because the patent teaches that the substance is usable to prevent multiple sclerosis. The person of ordinary skill in the art would have reasonably expected success because of the success of the in vivo testing against mouse liver apoptosis, which is also induced by the Fas ligand.

6. Claims 1-3, 6, and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Hughes and Crispe, J. Exp. Med, Vol. 182, 1395-1401, (1995) (Hughes); in view of Holoshitz et al, U.S. Patent Number 6,098,631 (the '631 patent); and D'Souza et al., J. Exp. Med., vol. 184, pp. 2361-

70 (1996) (D'Souza). Claims 1-3 describe a method of inhibiting an autoimmune demyelinating disease using an apoptosis suppressing substance, wherein the substance is a Fas antagonist, and wherein the substance suppresses Fas-Fas ligand binding.

Hughes teaches the use of a soluble variant of Fas to inhibit apoptosis induced by the Fas-Fas ligand interaction. Hughes, p. 1395. As a variant of the Fas receptor, those in the art would assume that the operation of the variant is to inhibit Fas ligand binding to the Fas receptor- thereby inhibiting apoptosis. Further, since the use of the variant is to inhibit the Fas-Fas ligand interaction, and the activation of apoptosis pathways, the variant is clearly a Fas antagonist. However, the reference does not teach the use of the variant to treat or inhibit autoimmune demyelinating diseases. The reference is describing a method of inhibiting the apoptosis of T cells.

However, the Fas-Fas ligand interaction was known in the art to be a part of the pathway leading to demyelinating immune diseases. See e.g., the '631 patent, col. 5, and col. 1, lines 9-20 (describing the pathway, and linking it to the autoimmune demyelinating disease multiple sclerosis), and D'Souza, pp. 2367-68 (linking Fas receptor and ligand binding with multiple sclerosis). Therefore, although Hughes does not teach the use of the variant to prevent autoimmune demyelinating diseases, it would have been obvious to one of ordinary skill in the art to use the variant as it is targeting the same ligand/receptor interaction that is responsible for causing multiple sclerosis. Cf. Hughes, p. 1395, ¶2, and D'Souza pp. 2367-68. Because multiple sclerosis is an autoimmune demyelinating disease, and because the Hughes variant is an apoptosis inhibiting substance- claim 1 would have been obvious to one of ordinary skill in the art. Further, the method of claim 3 would have been obvious because the Hughes variant inhibits

Fas-Fas ligand binding. Claims 6 and 7 would have been obvious because D'Souza and the '631 patent would have lead those skilled in the art to use the method taught in Hughes as a method of treatment of multiple sclerosis- an autoimmune demyelinating disease.

One of ordinary skill in the art would have expected success in the method because of the knowledge that the Hughes variant inhibited Fas-Fas ligand induced apoptosis. Since the method was effective in treating one form of Fas mediated immune disease, there would be no reason that a like treatment would be ineffective against another disease based on the same ligand receptor.

7. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being obvious over Nagata et al in U.S. Patent Number 6,348,334 (the '334 patent), in view of Holoshitz et al, in U.S. Patent Number 6,098,631 (the '631 patent) and Queen et al., in U.S. Patent Number 6,046,310 (the '310 patent). The listed claims describe a method of treating an autoimmune demyelinating disease (esp. acute disseminated encephalomyelitis and multiple sclerosis) using an apoptosis suppressing substance (esp. an anti-Fas ligand antibody).

The '334 patent teaches a method for treating autoimmune diseases such as rheumatism and SLE and AIDS, all of which are autoimmune diseases. (Col.25, lines 18-26) The method comprises the administration of anti-Fas ligand antibodies. See, col. 23, lines 52-55 (defining the antibodies used in the method as those targeting the polypeptides of the first and second aspects of the invention), and col. 3, lines 55-60, defining the polypeptides as Fas ligand and fragments thereof. Thus, the patent teaches the limitations of the claimed methods except for the treatment of an autoimmune demyelinating disease.

However, both the '631 and the '310 patents disclose methods and compounds usable for treating both rheumatoid arthritis and multiple sclerosis. See, U.S. Pat. '631, col. 1, lines 9-20, and U.S. Pat. '310, col. 2, lines 56-61. As exemplified by these two patents, the art recognized that the rheumatoid arthritis and multiple sclerosis diseases are related, and are treatable by similar methods. Further, the claimed method is targeting a specific protein ligand known to be involved in both of the diseases. Thus, one of ordinary skill in the art would have known to use the method disclosed in the '334 patent to treat multiple sclerosis as well. As multiple sclerosis is disclosed in the application as an autoimmune demyelinating disease (see claim 7), the disclosure of this disease also accounts for the generic claims 6 and 1-3.

Those of ordinary skill in the art would have had a reasonable expectation of success due to the success of the treatments in the above references. Since the described methods all relate to treatments targeting the Fas-Fas ligand interaction, and because they are all targeting related diseases, those of ordinary skill in the art would have expected the methods to achieve like results.

8. Claims 1-3, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lynch et al. in U.S. Patent Number 5,830,469 (the '469 patent) in view of D'Souza. These claims describe a method of treating an autoimmune demyleinating disease, especially multiple sclerosis, by the administration of a Fas antagonist that suppresses Fas-Fas ligand binding.

The '469 patent teaches the use of antibodies to the Fas receptor (therefore- Fas antagonists) that inhibit the binding of Fas ligands to the receptor, thereby inhibiting apoptosis. Col. 4, lines 48-54. The patent teaches that the antibodies may be used to treat the related autoimmune disease of rheumatoid arthritis, taught to be related to multiple sclerosis, and

therefore other autoimmune demyelinating diseases, in the references cited above. Col. 16, lines 3-14. The reference also teaches the use of a fusion protein comprising a binding domain of the Fas receptor that binds to the ligand (acting as a Fas antagonist) thereby preventing apoptosis. Cols. 10-11. Thus, the patent teaches multiple Fas antagonists, and that they may be used to treat autoimmune diseases related to the autoimmune disease of multiple sclerosis. However, the patent does not teach that the Fas antagonists may be used tot treat multiple sclerosis.

D'Souza teaches that the Fas-Fas ligand interaction is a part of the pathway leading to multiple sclerosis. P. 2368. D'Souza also teaches that Fas antagonists may have therapeutic applications. Id. Because D'Souza teaches that Fas antagonists may have such applications, and because the methods taught by the '469 patent are useful in treating the related disease rheumatoid arthritis, it would have been obvious to one of ordinary skill in the art to use the Fas antagonists disclosed by the patent in the treatment of multiple sclerosis (thus for autoimmune demyelinating diseases). Those of ordinary skill in the art would have has a reasonable expectation of success due to the success of the '469 patent's method in treating the related diseases.

9. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lynch et al. in U.S. Patent Number 5,830,469 (the '469 patent), in view of Aoyagi in EP document 0 285 883 (Aoyagi). These claims are to a method of treating an autoimmune demyelinating disease by administering a Fas- ligand antibody.

The '469 patent teaches the use of antibodies to the Fas receptor (therefore- Fas antagonists) that inhibit the binding of Fas ligands to the receptor, thereby inhibiting apoptosis. Col. 4, lines 48-54. The patent teaches that the antibodies may be used to treat the related

autoimmune disease of rheumatoid arthritis, taught to be related to multiple sclerosis, and therefore other autoimmune demyelinating diseases, in the references cited above. Col. 16, lines 3-14. The reference also teaches the use of a fusion protein comprising a binding domain of the Fas receptor that binds to the ligand (acting as a Fas antagonist) thereby preventing apoptosis. Cols. 10-11. Thus, the patent teaches multiple Fas antagonists, and that they may be used to treat autoimmune. However, the patent does not teach that the Fas antagonists may be used tot treat multiple sclerosis or autoimmune demyclinating diseases.

Aoyagi (the entire document) indicates that therapeutic agents for autoimmune diseases can also be used to treat autoimmune demyelinating diseases. See e.g., p. 2, ¶ 1, stating that the therapeutic agent of the invention may be used tin treating an autoimmune disease- such a multiple sclerosis which is an autoimmune demyelinating disease- indicating that there is no, or little, difference between the autoimmune diseases generally and autoimmune demyelinating diseases. Thus, it would have been obvious to one of ordinary skill in the art to use the antibodies of Okumura in a method of treating autoimmune demyelinating diseases because Aoyagi teaches that methods of treating autoimmune diseases may also be used in autoimmune demyelinating diseases.

A person of ordinary skill in the art would have had a reasonable expectation of success because the same receptor ligand are being targeted in both methods of treatment, and because targeting those molecules was effective in treating the related autoimmune diseases.

Information Disclosure Statement

10. The Information Disclosure Statement filed on Jan. 10, 2001 (paper no. 4) listed the Japanese document JP632306 as being accompanied by a translation. The translation was not evident in the file. Therefore, the document in full was not considered. However, it was considered to the extent on the abstract accompanying this action.

11. Those references included in the Information Disclosure Statements (papers3, 4, and 5) that are not in the English language have been examined to the extent of the abstracts that are in English.

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure is as follows:

EP document 0675200A1 discloses Fas antagonists (p. 10, lines 28-32) usable in treatments of apoptosis related diseases, and antibodies to Fas ligand likewise usable to treat apoptosis related diseases (p. 19, lines 9-23)

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
May 3, 2002

James C. Housel
5/6/02

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600